

## REMARKS

### **1. Notice Relating to Patent Term Adjustment**

The Office withdraws the Notice of Non-Responsive Amendment mailed January 7, 2009. The Office thereby acknowledges that Applicants' Response filed November 21, 2008, fully responded to the first restriction requirement, mailed May 22, 2008, and Applicants did not delay prosecution, within the meaning of 35 U.S.C. § 154.

### **2. Response to the Restriction & Election**

The Office now requires an election of a single species from both Group (A) and Group (B):

- (A) An OmpT protease 97<sup>th</sup> amino acid variant, where the species has one of the specific amino acid residues at the 97<sup>th</sup> position recited in claim 12-17, for example; and
- (B) A cleavage motif from the group consisting of the motifs described in claims 1-9, 11-14, and 26-35.

### **Election with Traverse**

For Group (A), Applicants elect the embodiment where the 97<sup>th</sup> amino acid is Met, *i.e.*, methionine (claim 13). For Group (B), Applicants elect the embodiment where the cleavage motif is SEQ ID NO: 12 (claim 11). Applicants elect **WITH TRAVERSE**.

### **Grounds for Traverse**

The present application is a National Stage application, so the rules and procedures governing restriction requirements must conform to the Patent Cooperation Treaty (PCT). *See* Article 27 of the PCT.

### **1. All the independent claims, claims 1, 8, 12-17, and 23 are novel over the cited art.**

The Office cites Okuno et al., "*Substrate Specificity at the P1' Site of Escherichia coli OmpT under Denaturing Conditions*," 66 BIOSCI. BIOTECHNOL. BIOCHEM. 127 (2002) [hereinafter "Okuno"] as allegedly defeating the novelty of claim 1.

Applicants traverse the objection to lack of unity, based on Okuno. Rule 13.2 provides that a group of inventions shall have unity of invention, where a technical relationship exists among the inventions “involving one or more of the same or corresponding special technical features.” Rule 13.2 further states: “The expression ‘special technical features’ shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.”

The Office alleges that the claims do not define a contribution over the prior art, because the cleavage site disclosed in Table 3 of Okuno, which has the sequence RLELYK<sup>↓</sup>RHHG, anticipates claim 1. The Office must have meant the sequence ELRLYK<sup>↓</sup>RHHG, which is the one actually disclosed in Table 3 of Okuno. Okuno’s cleavage site, however, does not anticipate claim 1. Among other things, claim 1 recites that “*a single basic amino acid is not situated at the P6 or P4 position.*” By contrast, P4 in the sequence ELRLYK<sup>↓</sup>RHHG in Okuno is R (*i.e.*, arginine), which is a basic amino acid. *See* Okuno, FIGs. 1-2 and Tables 1-3. Okuno accordingly does not teach each and every element of claim 1. The cleavage site in claim 1 thus defines a contribution over the prior art and constitutes a special technical feature that unites the claims, in accord with PCT Rule 13.2.

**2. Finding a lack of unity in dependent claims is improper without a careful consideration of whether the independent claims avoid the prior art.**

For the reasons above, the independent claims define a contribution over the prior art and contain one or more special technical features. Rule 13.2 is interpreted in the PCT International Search and Preliminary Examination Guidelines, revised March 25, 2004 [hereinafter “Guidelines”]. Guidelines, ¶ 10.06 provides that unity of invention is “considered in the first place only in relation to the independent claims.” If the independent claim(s) avoids the prior art, all the dependent claims have unity of invention. In particular, it does not matter if a dependent claim itself contains a further invention. Guidelines, ¶ 10.07. The Office must carefully consider the prior art to determine whether the independent claim avoids the prior art, *before* raising an objection over lack of unity as to the dependent claims. Guidelines, ¶ 10.08.

In the present case, for the reasons above, all the independent claims define a contribution over the cited prior art. Absent prior art defeating the novelty or inventive step of the

independent claims, a finding of lack of unity of invention with respect to dependent claims is prohibited. *See* Guidelines, ¶ 10.07. Accordingly, all the claims have unity of invention. *See* Guidelines ¶¶ 10.06-10.08. The present objection thus is unlawful and must be withdrawn.

To whatever extent the Office interprets Title 37 or M.P.E.P. to reach a contrary result, the Office's action is unlawful. Any rule or interpretation by the Office that conflicts with PCT Articles and Rules is reversed under 5 U.S.C. § 706(2)(A) as contrary to the law. *Caterpillar Tractor Co. v. Comm'r of Patents and Trademarks*, 650 F. Supp. 218, 219, 231 U.S.P.Q. 590, 591 (E.D. Va. 1986). The Office's reviewing courts do not accord substantial deference to the Office's interpretation that its own regulation is not in conflict with a treaty provision. *Id.*

**3. The species recited in the various Markush groups possess the same or corresponding special technical features as defined in PCT Rule 13.2.**

The Office independently alleges that the claims lack unity of invention because they are improper Markush groupings. Applicants also traverse this aspect of the objection for lack of unity. The Guidelines state (¶ 10.17) that a Markush grouping for alternatives of chemical compounds has unity of invention when the following criteria are fulfilled:

- (A) all alternatives have a common property or activity, and
- (B)(1) a common structure is present, i.e., a significant structural element is shared by all of the alternatives, or
- (B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.

**3.1. Cleavage Sites**

The Markush claims reciting species of cleavage sites have unity of invention. All the recited cleavage motifs have the common property or activity that OmpT protease cleavage efficiency at P1-P1' is enhanced, so all the species comply with criteria (A) above. The Office then must consider whether the species belong to a "recognized class of chemical compounds" under (B)(2), above. This criteria is met under the PCT when the species can be substituted one for the other with the same intended result:

(c) In paragraph (a)(B)(2), above, the words “recognized class of chemical compounds” mean that there is an expectation from the knowledge in the art that members of the class will behave in the same way in the context of the claimed invention. In other words, each member could be substituted one for the other, with the expectation that the same intended result would be achieved.

In the present case, each species shares the functional property of an OmpT protease cleavage site. Clearly, the species of OmpT protease cleavage site in any one Markush claim will behave in the same way in the context of the claimed invention, namely, as an OmpT cleavage site. So each species complies with the (B)(2) prong of the analysis above.

### **3.2. OmpT Proteases**

The same analysis mandates a conclusion that claims alternatively reciting species of OmpT protease also have unity of invention. The OmpT protease 97<sup>th</sup> amino acid variants have the common property or activity of altered substrate specificity, relative to the wild-type OmpT protease, which relates to the substitution at the 97<sup>th</sup> amino acid position. *See* Specification, p. 27, last paragraph, referring to Kramer et al., “*Identification of Essential Acidic Residues of Out Membrane Protease OmpT Supports a Novel Active Site*,” 505 FEBS LETT. 426 (2001). Thus, each Markush claim directed to OmpT protease 97<sup>th</sup> amino acid variants complies with prong (A) of the analysis in the Guidelines. Likewise, each Markush claim directed to wild type OmpT proteases satisfies prong (A), because each species has the common property or activity as an OmpT protease.

The proteases clearly all share a “significant structural element.” An OmpT protease 97<sup>th</sup> amino acid variant, for example, is structurally the same as its wild type counterpart, except for one amino acid substitution. Further, within a single Markush claim, all the protease variants will behave in the same way in the context of the claimed invention, namely, as an OmpT protease. So the species comply with both the (B)(1) and (B)(2) prong of the analysis above.

The Office alleges that the cleavage sites “do not share a common structure or function, as defined by the ability to be cleaved by any [sic: all?] encompassed protease.” The Office also alleges that the proteases do not share a common structure or function because they have different “cleavage specificities,” with reference to Table 1 and Figure 3 of the specification.

The Office appears to require that species must quantitatively functionally equivalent in the same Markush claim or between Markush claims. First, unity of invention of a Markush claim is determined independently of other Markush claims in the application under PCT rules. *See* Guidelines, ¶ 10.17. Second, there is no requirement under PCT rules for quantitative functional equivalence of each species to find unity of invention of a Markush claim. *See* Guidelines, ¶ 10.17. The Office has no authority to add additional requirements inconsistent with PCT rules and procedures. *See Caterpillar Tractor*, 650 F. Supp. at 219, 231 U.S.P.Q. at 591. Finally, to the extent the Office argues that the claims can be united by only a single special technical feature, the Office contradicts PCT Rule 13.2.

Applicants accordingly respectfully request reconsideration and withdrawal of the species election requirement and consideration of all the claims on the merits.

### **CONCLUSION**

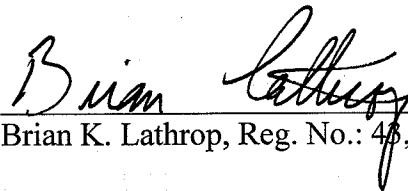
Examination on the merits is requested. If there are any other fees due in connection with this filing, please charge the fees to our Deposit Account No. 50-0573. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

**DRINKER, BIDDLE & REATH LLP**

Dated: April 3, 2009

By:

  
Brian K. Lathrop, Reg. No.: 46,740

**CUSTOMER NO. 55694**  
**DRINKER, BIDDLE & REATH LLP**  
1500 K Street, N.W., Suite 1100  
Washington, D.C. 20005-1209  
Tel: (202) 842-8800  
Fax: (202) 204-0289